baseline and regular intervals. And have all of the specular microscopy results assessed at a central location for the sake of comparability of results.

You'd want the sample to reflect the diversity of patients and implanting physicians so that you can get at the real-world aspects, and follow as many sample patients as possible for 30 years, or whatever time is deemed proper.

And the advantages of doing this would be that the follow-up would be concentrated at expert centers, and there would be central reading of the counts. There would be early warning of cell count decline, and it could be used to detect other adverse events, such as cataract or the other outcomes.

Disadvantages are you need aggressive persuasion of the sample patients to come in for their visits, and it would be more expensive. Is there any questions?

DR. WEISS: Okay. Thank you. What I'd like to do is sort of cut to the chase, because I feel we're -- the reason we're raising this question, and I couldn't delay it as long as I wanted to, to get to

other issues, was because I feared we were going to go around in circles, and that's what's begun to happen. So what I'd like to do is just address ourselves to the issues of safety to sort of hone down on what our concerns are, as bespeaks the endothelial cell count.

What I'd like is, those who are concerned that any of these patients, even if they didn't have any other surgery, could develop corneal decompensation, corneal edema from this procedure, I'd like a show of hands for those members of the panel who are concerned that from the data they've seen, these patients could develop corneal edema, at any point down the line. Are you concerned that that could happen?

(Vote taken.)

DR. McCULLEY: That's an open-ended question.

DR. WEISS: That is an open-ended question. So that's true, it is an open-ended question, Jim. Then the second question I have for those of you who have that concern, do you think a large percentage of patients -- are you concerned that

a large percentage of patients could develop corneal edema from just the implantation of this device?

(Vote taken.)

DR. WEISS: So you have -- no one has any ideas on -- so is that what the safety concern is here? Because if that's what the safety concern is, then I think we're talking about specifically the loss of endothelial cells, and we should address ourselves to doing a study that addresses that particular concern, which is the loss of endothelial cells. Is that the concern on the panel, is the loss of corneal endothelial cells?

DR. MATHERS: That's one concern.

DR. WEISS: That's one concern. Okay. So let's address ourselves to that concern. What -- is there any problem -- why -- would not following the cohort of 306 patients for up to a five year period of time to see if there was stabilization with an additional year, address the concern of loss of endothelial cell count, or why would that not address that concern? Dr. Mathers.

DR. MATHERS: It might or might not,

depending on how the data came out. It would certainly help.

DR. WEISS: Dr. Bradley.

DR. BRADLEY: It seems we've had a discussion of do the data stabilize or do they not stabilize. And I wonder whether that's the appropriate question we should be challenging the Sponsor and the FDA with, in terms of this post -- possible post-approval analysis. Mike Grimmett a couple of years ago suggested 1.5 percent per year loss was okay. The current data is 1.8 percent, I believe. Is that what Marian said? A simple statistical question is whether or not the data show a significantly greater decline than the decline that is considered safe. If the decline is concerned safe as 1.5 percent per year, it becomes a statistical question to analyze the data. And it may take five years to do that, to show whether or not the data are declining not significantly more than this supposedly safe decline rate of 1.5 percent. So the issue of stabilization versus not, doesn't seem to be the issue here. It seems to be whether or not the decline is

greater than what is considered safe. And that becomes a very straightforward statistical question, which surely the Sponsor and the FDA could sort out.

DR. WEISS: Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: More from a public health point of view, you could state it the other way. Right? In other words, you might want to demonstrate that it's at least that safe, you know, that it's no greater than 1.5, rather than just that it's not statistically different than 1.5.

DR. BRADLEY: I think that surely that's all one is able to do, to say whether it's statistically different or not.

DR. BANDEEN-ROCHE: Right, but you might want to reverse the Type 1 and Type 2 error, and require evidence that the rate is lower than 1.5, rather than just saying it's not statistically greater.

DR. WEISS: Dr. Rosenthal, could we have some help, because I could see we're getting nowhere here. And we're taking a long time to get nowhere. Do you have any suggestions for the panel?

DR. ROSENTHAL: The panel has to decide whether they want follow- up of these patients before they give an approvable. They can give approvable with conditions, and the conditions can be follow-up of the patients before it goes on the market, or after it goes on the market. And give not-approvable because then that -- with the same -- of course, in the not-approvable situation, it would be because they don't have the data before they give the approvable.

DR. WEISS: At the present time, as concerns the issue of endothelial cell loss, can the panel members who feel there is not enough information right now to make a decision on safety before this is released into the market, could raise their hands. Dr. Matoba.

DR. MATOBA: What about if we vote on whether panel members would be satisfied if Sponsors were to follow for an additional amount of time, the patients for whom they have pre-op endothelial or specular microscopy, and then vote on whether it should be four years or five years.

DR. WEISS: Well, the first question that

we need to answer, and which the FDA is bringing forth to us, is if we don't have that data, I'm getting -- I'm not getting a sense from the panel whether that data can be given after this is released into market, or it's a condition for --

DR. MATOBA: But I think we can agree on whether we want --

DR. McCULLEY: Vote on it.

DR. MATOBA: I think we can agree on whether we want the data or not. And then we can decide whether we would be willing to approve or not approve.

DR. WEISS: Fine.

DR. McCULLEY: We want the data.

DR. MACSAI: We want the data.

DR. WEISS: Everyone --

DR. MATOBA: Okay. So but then do we agree that if they follow those patients who had pre-operative specular microscopy that's adequate, or are we going to ask for something --

DR. WEISS: Well, why don't we just break this down into simple points. Is everyone in

agreement that we would want to get at least five year data for the patients who've had pre-operative specular microscopy? Those who are in agreement with that, could you raise your hand?

(Vote taken.)

DR. WEISS: Does anyone want longer than five year specular microscopy or would like the FDA to determine the length of the study depending on what the results of five year microscopy? Depending on the results of the five year microscopy, that would determine the length of that particular study.

DR. MACSAI: Jayne, we can request that that be brought back to panel, that five year data for review, or the FDA can review it.

DR. WEISS: Well, I think FDA will look at it. I don't think that has to be -- if we're -- well, whether or not it got brought back to panel depends on whether this gets approved with conditions or not, so that's -- am I correct, Ralph, on that?

DR. ROSENTHAL: Yes.

DR. WEISS: Yeah. Okay, so we -- I think --

DR. ROSENTHAL: It's whether you do not approve it.

DR. WEISS: Then it would come back for another go around. So the panel is in agreement that they would like the cohort that's had pre-operative specular microscopy, have another specular microscopy done at five years time, and then --

SPEAKER: Annually until five.

DR. WEISS: Annually until five years, and then have the FDA determine how long after, in terms of those results. Now on that basis, what I need to find out from panel is, would that be information that is needed before this gets approved? And how many of you would require that information before you would feel comfortable voting for saying that this is a safe device?

DR. GRIMMETT: Jayne, there's two issues there. How many would feel comfortable just having year four, or needing both, so there's two parts to that.

DR. WEISS: No, I don't want to break it down any further. We're splicing -- I'm stating the

question. Actually -- okay. I don't - - if we keep on deviating, we're going to be here until tomorrow, which I don't -- I'd just like to hone in on this particular question. We've talked about up to five years. We want specular microscopy. We've talked about perhaps extending that, depending on what that data shows. What I just want is a show of hands from the panel, is this needed to vote for approval? Would you need this data before you would feel that this is approvable, with or without conditions?

DR. GRIMMETT: All the way to five, inclusive of everything, needing five.

DR. WEISS: So, Mike, you would need five -- you would need an additional year data before you would approve this?

DR. GRIMMETT: No. I would need four year data as a condition of approval, in order to approve it.

DR. WEISS: Okay.

DR. GRIMMETT: With five year being a post-market surveillance.

DR. WEISS: Fine.

DR. GRIMMETT: That's my position.

DR. WEISS: Fine. Does anyone have a position different than what Dr. Grimmett said? Dr. Sugar.

DR. SUGAR: I would suggest conditional approval with continued acquisition of that data up to five years; that is, this would be a marketable device once the agency approves it, while we're still acquiring that data.

DR. GRIMMETT: When they see four year data, -- just as a clarification, Dr. Sugar, when the FDA sees four year data, and feels that it shows a reasonable level of stability, then it can be approved.

DR. SUGAR: Well, no. It would still -- it would be conditionally approved, so it would be marketed now.

DR. GRIMMETT: Oh, so your's are all post-market. Year four and year five are post-market.

DR. SUGAR: Unless I misinterpreted Dr. Bright's statement, that we could conditionally approve it, and it could be marketed with the

condition that that data continued to be acquired; that is, this is a marketed device --

DR. GRIMMETT: Isn't that post-market surveillance?

DR. ROSENTHAL: You can do it two ways. You can require the data to be submitted to us before it can go to market, four years, five years, four years only, four and five years, or you can say it can go out right now, but once it's out in the marketplace, we have to get the data at four and five years.

DR. SUGAR: The latter is --

SPEAKER: You want post-market surveillance. You are in agreement on that.

DR. SUGAR: Post-market acquisition of data through five years, with it being conditionally approved.

DR. WEISS: So I'm getting a sense from the panel right now, there are these two different choices. But from what I'm hearing from the panel, they would feel comfortable with the post-market surveillance, post-market --

DR. McCULLEY: Get a vote on the two.

DR. WEISS: Dr. Bandeen --

DR. GRIMMETT: Four years before it gets out with continued post- market to five. That's choice one. Choice two is, let it go now and do post-market surveillance on four and five when it's already out in the market. That's choice two. Vote for one or two.

DR. WEISS: Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: Am I correct in presuming that by the time the four year follow-up is complete, there will be some five year data?

DR. WEISS: Yes.

DR. BANDEEN-ROCHE: So that's another --

DR. WEISS: So why don't you state the first choice, and we can have panel --

DR. GRIMMETT: Let's state the second. How many would vote for approval now with the current existing data, with post-market surveillance of endothelial data at four years and five years?

(Vote taken.)

DR. GRIMMETT: That was your choice, if I

stated correctly. That's enough.

DR. ROSENTHAL: How many were there?

DR. WEISS: And how many would vote for -- restate the first one.

DR. GRIMMETT: For gathering the four year data now as a condition of approval, and if satisfactory by review of the FDA, then approve it, and then continue post-market surveillance out to year five.

(Vote taken.)

MS. THORNTON: It was six to five.

DR. GRIMMETT: You want to take it again?

DR. ROSENTHAL: Yeah, could we.

DR. GRIMMETT: Take it again.

MS. THORNTON: It was six to five.

DR. GRIMMETT: Which way?

DR. ROSENTHAL: Could we have the other first?

DR. WEISS: Now I just want to clarify the four year data that we're trying to get, you have a continual number of patients who are getting four year data, so when will you get this four year data? At

what time point would you --

DR. ROSENTHAL: We need you to tell us.

DR. WEISS: I know it's ongoing, so if the -- so you would -- so the panel --

DR. ROSENTHAL: Ten more eyes, 20 more eyes?

DR. WEISS: How many --

DR. ROSENTHAL: All the eyes. It's up to you.

DR. WEISS: Okay. So then I would -- I'd like the panel to understand that if they went with, I believe it's the first option, it's undefined when that condition would be met. Am I correct?

DR. ROSENTHAL: Do you want to explain?

DR. WEISS: When would that condition that all the four year data for all these patients would be met? Because we also have to realize that they only have four year data on 57 patients at the present time, so how many more patients would they be able to get four year data on?

MS. LOCHNER: At the present time, they obviously have more than that number. That cut-off on

the database happened a couple of months ago, so as we speak, more and more people are reaching four years. I think the Sponsor can address, you know, the issue is when was the last patient enrolled. When will the last patient be out to four years in that cohort, and so they'll know exactly when they'll have the complete group.

DR. MACSAI: It's December of 2006.

DR. WEISS: What I would like to know from --

MS. LOCHNER: No.

DR. WEISS: Yeah. I'd like to know from Dr. Gray statistically what number would you need, or what number of patients would you need to have four year data before you feel that you could make a - - Dr. Gray, do you have any comment on finding four year data for all the remaining patients helpful?

DR. GRAY: Helpful?

DR. ROSENTHAL: Oh, no. He's not to give you any --

DR. GRAY: I can't answer that kind of a question without a lot more information. I mean,

that's a difficult --

DR. WEISS: How many --

DR. GRAY: I can't do it off the top of my head. I'm sorry.

DR. WEISS: From the FDA, how many -- the last four year data would be coming back when? When would be the -- Sponsor, please.

DR. LAMIELLE: Helene Lamielle. December, 2006.

SPEAKER: What did she say?

DR. WEISS: December, 2006. Dr. Macsai.

DR. MACSAI: Dr. Lamielle, is that -- because I -- that's what I thought too, but now I'm rethinking it. Is that the last person enrolled, or is that the last person with specular microscopy? I don't get that clear.

DR. LAMIELLE: That's the last person on the whole.

DR. MACSAI: But when was the enrollment of the 306 specular microscopy patients completed?

DR. LAMIELLE: We have to look at the data, when the last microscopic specular patient was

enrolled.

DR. MACSAI: Okay.

DR. LAMIELLE: But the specular microscopy data have been done all along the study, so there is no reason -- it's earlier than the rest of the cohort.

DR. WEISS: So I would just like clarification from the panel members who would require this data that perhaps may go out to approximately two years from now in order to release this into the market. I would presume that you would want to delay approval of this for two years, or more than two years, because you have concerns about safety because of the specular microscopy data. Am I correct -- for those of you who voted for Option 1, am I correct on assuming that's the cause of the vote in that direction? Dr. Mathers?

DR. MATHERS: Concerns about the endothelial issues - I'm sorry.

DR. WEISS: Yes, because you would be delaying the vote, or it would have to come back to -- you'd be delaying this for more than two years, because you have concerns about safety as regards to

the issue of the findings on the specular microscopy.

DR. MATHERS: That is precisely the problem, and I think that it is a very significant issue, and we should know more before we get approval. That's why I voted for conditional approval, that we need to know this before we approve it.

DR. WEISS: Yeah, Donna.

MS. LOCHNER: I was just going to say, it is possible that as the Sponsor theorized that the rate is essentially going, you know, dramatically down at four years, that the data will have sufficient power before the last of the patients are enrolled. So if what they're theorizing is true, they may not have to wait as long as you're saying to have sufficient power to show that the loss is decreased from the three year point.

However, in a worst case situation, maybe they'll need all their data, and have to wait that long. But if their theory is true, one would expect that they would be able to have sufficient power much earlier than that.

DR. WEISS: So the panel could say that

they would want acquisition of four year data until -- for the number, until which point the FDA deems that they can determine with certainty that the data shows stability, at which point then that would be the condition that would be met for it to be released into market.

MS. LOCHNER: Certainly. And no matter what the panel or FDA says, the sponsor will push that point in any case, so you don't have to worry --

DR. WEISS: Dr. Mathers, and then Dr. Bradley.

DR. MATHERS: I would like the condition to be achieved, such that at the end of the lifetime of the device, that the patient would still have 1500 cell count.

MS. LOCHNER: Right. And if you just use the data the sponsor has, you can do that calculation and see where they are.

DR. MATHERS: That's correct. It is a lower rate than 1.5 percent per year.

MS. LOCHNER: We understand.

DR. WEISS: Dr. Bradley.

DR. BRADLEY: Again, just to clarify, the stabilization, absolute stabilization is not the gold standard here. It is the rate which is -- rate of decline which deemed safe. And we've got a 1.5 is okay, and a 1.5 is not okay. so there is some debate about what the rate actually is.

DR. WEISS: Dr. Grimmett.

DR. GRIMMETT: Let me clarify. That 1.5, the figure came about at last year's meeting due to the fact that in looking at what would be a sample size needed to show a specific rate of cell loss. And if we set the bar too low, the sample sizes would have to be enormous. It wasn't that 1.5 was deemed a safe level. It was that 1.5, if you wanted to screen that they were under that, your sample sizes could be reasonably sized so it wouldn't be onerous. That's where it came up.

DR. WEISS: Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: I just wanted to say that I agree with this discussion that's been happening in the last couple of minutes and, you know, just so long as we also keep in mind representation,

as well as just power. You know, that we're not -- we don't have an overly selective group, both sufficient numbers, and decently representative of the whole cohort.

DR. WEISS: Dr. Macsai.

DR. MACSAI: I'd like to speak in favor of my disagreement with the majority of the panel. We had a presentation by Dr. Edelhauser who's deemed internationally as an expert in the field of endothelial cell data of all sorts, and we've seen that the pleomorphism and polymegathism are pretty darned good here, and they're stabilizing. And then we looked at that they counted 90 cells, but probably 100 to 150 cells would have been better. And there's a lot of room for error in the 90 cell count, and now we're arguing about 1.8 versus 1.5, versus 2 percent. Where, if you looked at the confidence interval of those numbers, and then took a confidence interval of those counts, and then, you know, multiplied it by all those factors out, I think you'd wash this whole thing away.

You know, I'm concerned as everyone, and

I started out my whole review as saying that this -- we don't want to create ORC - I can't - a situation with a lens - excuse me - take that from the thing - a lens that might cause endothelial cell decompensation, but we have a device that's really effective, probably more effective than what's out there. And I know safety is really important, and you're talking to Mikey who doesn't like anything here, but I mean, do we really want to wait until 2006?

We approved these contact lenses when we already had your study saying, you know, they're dangerous. Okay?

DR. WEISS: I think at this point we have the data, and everyone, I think, has their opinions or has quite a few opinions. And at some point, this may come to a very close vote. But I think the information is out there, and we all have our perspective on, and we still have a couple of questions. And I don't want to tell you how many hours behind we are, so we're going to -- I think we have the information on endothelial cells. We're

going to end up putting it to a vote, and when it gets put to a vote, and what I'd like to do is go on to a non-controversial topic, like cataracts. I bet the Sponsor didn't think that was going to be the non-controversial portion.

DR. EYDELMAN: Question 2(a) - "Do you believe that the three year follow-up is sufficient to establish a lens pacification profile associated with this device? If not, what is your recommendation?"

DR. WEISS: Dr. Macsai.

DR. MACSAI: It's sufficient.

DR. WEISS: I think the panel has gotten beaten into submission.

DR. SUGAR: I think we should ask for post-marketing acquisition of data on cataracts that accrue in this five year period while we're looking at their endothelium.

DR. WEISS: Sounds good. Dr. Schein.

DR. SCHEIN: As I said before, I'm more concerned about cataract and retinal detachment, than I am about the cornea. Because although it is uncertain on endothelium, there has not been

progression to any clinical disease, while there has been, in a relatively short time period. I frankly don't believe most of the cataract rating. I don't disbelieve it because I think investigators are dishonest, but I know, and it's well-published, that using clinical grades, whether it's the LOC system or the Wisconsin system, is incredibly unreliable. You need a photographic standard to really believe it, and that may be why there's such variation between Canada, these investigators, site- to-site, and Dominican Republic, and maybe more than just position skill. So I think this is a real issue. People who get cataract surgery, their myopes. They're going to have the eye entered twice, retinal detachment rate will behave accordingly, so I don't think this is adequate information to establish a lens opacification profile. You need a larger sample and representative surgeons.

DR. WEISS: Well, certainly I would think it would be not difficult if we're going to be getting data at four years, five years, to include cataracts in that.

DR. SCHEIN: It's not a large sample, and

it's not a representative group of surgeons.

DR. WEISS: Dr. Sugar had mentioned considering IOL removal if there's progression of cataract formation. Did anyone want to put that in the labeling, as well? And that goes later on, but I have it.

DR. SUGAR: I don't think it's --

DR. WEISS: Is that what you said, Joel, or is --

DR. SUGAR: No. I expressed lack of information --

DR. WEISS: Lack of data.

DR. SUGAR: -- on what the toxicity of the removal event is, in terms of, do cataracts get worse after you take the lens out? I don't know.

DR. WEISS: So you --

DR. SUGAR: And I don't think the Sponsor has sufficient numbers within this cohort to give us an answer that would satisfy me.

DR. WEISS: So you're not going to ask the Sponsor for an answer -- it's a question that remains and will stay unanswered. Or would you like to ask

the Sponsor --

DR. SUGAR: Again, if the Sponsor has data on -- you know, certainly if they find that removing the IOL is cataractogenic, obviously, they need to let us know that. And I assume that they're mandated to let us -- to let the FDA know that as an adverse event.

DR. WEISS: As part of the -- Dr. Rosenthal.

DR. ROSENTHAL: Unfortunately, the adverse event issue, if they're informed of it, they are mandated to let us know. But if they are not informed of it, unless the physician reports it through the MDR system, we will never know about it.

DR. WEISS: Well, we can ask them at this point if they have the information to let the FDA know. Is that correct?

DR. ROSENTHAL: Well, at this point you have the information because it was submitted in the PMA.

DR. SUGAR: No. We don't have information on whether removing the lens halts progression or

induces progression of whatever opacities were there.

DR. ROSENTHAL: No, you don't have that.

DR. WEISS: So we can ask them for that information, and that's - - if they have it.

DR. ROSENTHAL: When? When do you want them to give it to us?

DR. WEISS: If it was -- if the panel wanted, that could be a conditional, could it not?

DR. EYDELMAN: I just want to make it clear.

DR. WEISS: Yes.

DR. EYDELMAN: Are you trying -- there's no data from the PMA cohort that you're discussing obtaining the data from post-market, or what exactly --

DR. WEISS: I think Dr. Sugar is talking about the patients who've already had this done. Am I correct?

DR. SUGAR: Well, then the number is too low.

DR. EYDELMAN: Yes.

DR. WEISS: Okay. So then do you have --

is there a statement you want to make, or is that just sort of a wish list that's not going to get answered?

DR. SUGAR: I guess I don't know how to make the statement about the statement, but yes.

DR. WEISS: Dr. Eydelman, do you have a suggestion on how to make a statement about a statement?

DR. EYDELMAN: If you want to find out the specific rate, you need to collect data. If you want to have a general warning, a precaution about lack of data, you can do that in labeling. Those are the two options.

DR. SUGAR: I guess both is what I would like, which is to find out if -- and I don't know how you find this out. Assuming, as I think we are, that this is a low frequency event, it's going to be hard to acquire that data in any very short period of time. It would be nice to know what appropriate recommendations are for dealing with lens opacification in these patients that is not visually significant. Does removing the implant cause progression or halt progression?

DR. ROSENTHAL: Ralph Rosenthal. I think at this point in time, all we can do is put a warning in saying that you do not know what the effect would be on the cataract that develops following implantation when you explant it.

DR. SUGAR: Then I think the labeling should reflect there is a lack of data on the impact of removing and/or replacing the lens on the endothelium and on the lens.

DR. WEISS: Fine. Dr. Matoba.

DR. MATOBA: Well, okay. I hate to ask this question because of labeling conditions, but is someone keeping track of all the labeling questions?

DR. WEISS: I am, as well as Dr. Mathers, I hope. Any other issues about cataract?

DR. SUGAR: I guess I raise the other one, the axial length measurement. Is axial length measurement accurate with the lens in place? And I don't know how to deal with that in this.

DR. EYDELMAN: That is actually something we can ask the Sponsor, and work out the proper -- that is the easiest of the issues. We have not heard

the answer to Question 2(a).

DR. WEISS: So the question -- Question 2(a) is - "Do you believe a three year follow-up is sufficient to establish a lens opacification profile associated with this device"? All of those who feel that it is, and would like to answer yes, please raise your hand.

(Vote taken.)

MS. THORNTON: We have eight.

DR. WEISS: So it's a majority, not unanimous, but a majority. And we'll go with the majority. B. Question B is --

DR. EYDELMAN: "In light of the findings, they believe surgeon experience to have be an important factor in ASC development secondary to surgical trauma. If yes, they believe that future users of this lens should be required to undergo special training."

DR. WEISS: So I think that there was a consensus that there should be special training. Would the FDA need to know from us what type of special training, or you can determine that with the

Sponsor? Dr. Macsai had mentioned -- Dr. Sugar and Dr. Macsai, I think both had mentioned mandate - perhaps proctor for early cases, but that's something that you all can determine with the Sponsor, so we do not have to get involved in that.

DR. ROSENTHAL: I think I should clarify. We can mandate training. We generally do not mandate what type of training.

DR. WEISS: So would it be acceptable to the panel that training or some sort be mandated?

(Vote taken.)

DR. WEISS: Fine. Dr. Macsai had brought up tracking and recalling. If there were multiple surgical problems with a physician, I would assume that would be too burdensome and beyond the usual scope that we advise. Am I correct on that?

DR. EYDELMAN: Yes.

DR. ROSENTHAL: I've never heard it recommended before. If the sense of the panel is that that's what they feel is reasonable, we can ask the agency -- well, we are the agency. We can ask higher up in the agency what their feeling is about the

recommendation. We may not take it, and we may take it.

DR. MACSAI: Jayne, can I clarify?

DR. WEISS: Dr. Macsai, yeah.

DR. MACSAI: The recommendation really wasn't to the agency, it was to the Sponsor. The recommendation was simply to the Sponsor, that if there's a disproportionate number, I assume these are not - - these are going to be consignment lenses, and if somebody, you know, keeps ordering new ones, and keeps sending back ones they implanted wrong, or they tore upon implanting because they can't manage to get them through the shooter, red flag. Go retrain that person. Rescind their certification. As simple as that.

DR. WEISS: So the agency can take that under advisement. Okay. The Sponsor. C.

DR. EYDELMAN: Has to do with recommendation for replacement of ICL.

SPEAKER: I think we dealt with that at one point.

DR. EYDELMAN: Yes, we did.

DR. WEISS: WE did this one. Okay. What was the answer?

SPEAKER: We don't know.

DR. WEISS: We don't know. Always nice to have definitive answers for the agency. Question 5, "Do the safety and efficacy outcomes support approval of the STAAR ICL for the eyes with the following pre-operative manifest. (A) is minus 3 to minus 7." Now one thing I will point out, obviously, the results in these patients were much better. But then again, you might -- the panel might determine the risk benefit ratio is also a little bit different because there are effective treatments in these patients. A minus 3 has a whole choice of treatments, where a minus 15 does not. But having added that introduction, I'd like a vote. For those who agree that the safety and efficacy outcomes, safety and efficacy support approval for eyes with minus 3 to minus 7 - if you agree, vote with your hand in the affirmative.

(Vote taken.)

MS. THORNTON: I've got one, two, three,

four.

DR. ROSENTHAL: No, there are five.

MS. THORNTON: Five. Where's the other one? Tim, keep your hand up.

DR. ROSENTHAL: There's one, two, three, four, five.

DR. WEISS: Okay. Five out of 11.

DR. ROSENTHAL: No. You have to vote.

DR. WEISS: Why don't we have --

DR. ROSENTHAL: There has to be another vote.

DR. WEISS: Five people are voting in the affirmative. For those who disagree that safety and/or efficacy do not support approval for minus 3 to minus 7, can you vote? They disagree.

DR. ROSENTHAL: Please vote. You can abstain. Please vote either yes, no, or abstain.

DR. MACSAI: Minus 3 to minus 7.

DR. ROSENTHAL: There's four against.

DR. WEISS: This is a no vote. Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: We're taking

everything into account, including the discussion on --

DR. WEISS: Every single thing.

DR. BANDEEN-ROCHE: -- endothelial cell count. Right?

DR. WEISS: Everything. Safety and efficacy.

DR. EYDELMAN: Well, you're voting both ways.

DR. WEISS: Okay. What are we voting now? Okay. Let's have a vote again. Those who agree that safety and efficacy outcome support approval for minus 3 to minus 7 - those who --

DR. GRIMMETT: With or without the prior endothelial concerns. Are you separating that out? Are you concluding it, the endothelial safety issue?

DR. WEISS: Yes.

DR. GRIMMETT: We already went over, or are you separating it out?

DR. SUGAR: With the condition, I assume.

DR. GRIMMETT: Point of clarification.

DR. WEISS: Well, with the conditions of

-- let's -- if you want to break it out, let's break it out into needing the four year data as a condition of approval. And then we'll have a vote for not needing the four year data, but as a condition of approval having it --

DR. SUGAR: We just did that. We voted that way.

DR. WEISS: So let me -- I'm going to defer to FDA. Since we've done, how do you want this phrased at this point to give you any information?

DR. EYDELMAN: Okay. I will assume that you're not expecting to stratify the four year data by preoperative refractive bins, because then we'll never have enough. So, therefore, you have to take into consideration then endothelial cell data as you know currently. And assuming that overall four year data will be looked upon until this device is marketed, do you consider that safety and efficacy -- do they support approval for minus 3 to minus 7?

DR. WEISS: So for those of you who require that four year data before as a condition of approval, four year data on the rest of the cohort as

a condition of approval, do you believe it's efficacious for minus 3 to minus 7?

DR. COLEMAN: Excuse me, Jayne. Can I have safe and efficacious.

DR. WEISS: Safe and -- is that --

DR. GRIMMETT: For everything else but the endothelium.

DR. WEISS: No. Once you have your four year data, you're going to have your four year data as a condition of approval.

MS. LOCHNER: Can I say something?

DR. ROSENTHAL: Can I clarify?

DR. WEISS: Yes, please clarify.

DR. ROSENTHAL: Are you -- do you want -- what -- do you want to limit the power -- the refractive error for which this device should be used or do you not?

MS. LOCHNER: And to say that another way, I think the panel already voted on the endothelial cell issue. And the motion seemed to carry that the four year data would be obtained pre-marketly.

DR. ROSENTHAL: That was a straw vote, and

--

MS. THORNTON: Would you please use the microphone.

DR. WEISS: It would be a straw vote. I'm sorry. Maybe it wasn't in the --

DR. ROSENTHAL: It was a straw vote, and you still don't know what the ultimate vote will be, and what the conditions will be.

MS. LOCHNER: But I think we want you to set aside the endothelial cell issue at this time, and speak to the refractive ranges.

DR. WEISS: So we're speaking now basically of efficacy. If we're speaking about --

MS. LOCHNER: No, safety and any other --

DR. WEISS: Safety and endothelial cell data, and efficacy. We're trying to get at whether, setting aside the endothelial cell issue, which we already had a straw vote on, and we assume that that issue wouldn't change based on the refractive ranges. Setting that aside, are there additional concerns that might make you vote differently by the different refractive ranges? Dr. Coleman.

DR. COLEMAN: Yeah, but one of my issues that hasn't been addressed, because we've been voting on safety based on corneal endothelium, is the safety related to glaucoma, and also the lack of gonioscopic data. And one of the things that I need in terms of for my feeling, the safety of this procedure is having post- operative gonioscopic evaluations on the cohort in this PMA. And that information is not available.

DR. WEISS: Okay. I would like to -- I'm getting disturbed how the proceedings are going. I would like to emphasize, this is reasonable safety and efficacy. I mean, there -- I think it would be nice to have gonioscopy, and I think there were other parts that could have been included in the study. But with all fairness to the sponsor, at the point that this study was approved, it was approved with the input of the agency, so we can't hold them up to a higher requirement, which would be nice, but it's not fair for information that we've subsequently gathered.

With the data that we have, and that the agency required from them, and that they performed, do we have reasonable safety and efficacy? I would be

disturbed if at this point this was -- it was not approved on the basis they didn't have post-operative gonioscopy because that was not a requirement that the agency made, and there is nothing in particular --

SPEAKER: That was a requirement that the panel --

DR. WEISS: Well, the panel made that, but that was not a binding requirement. I mean, can the agency comment if I'm out of line here?

DR. COLEMAN: It's not in the study, but the thing is that they could -- this is Dr. Coleman again - excuse me. I thought that you could when you're doing the four year reviews or the five year reviews of these individuals, same with conditional approval, but they could also have gonioscopy by the surgeons to see how the angles were doing, whether there's pigment deposition --

DR. WEISS: No, I think that --

DR. COLEMAN: So it's definitely doable, even now in this current cohort. It's just that information hasn't been obtained. And you have an increased rate of interocular pressures of about -- in

three years in this cohort about 6.8 percent of the cohort has a pressure elevation of more than 5 millimeters of mercury from baseline. If you believe the ocular hypertensive treatment study, that's associated with a 50 percent increased risk of glaucoma in these young individuals. And so specular microscopy

DR. WEISS: What percent of higher myopes would be expected to get glaucoma?

DR. COLEMAN: That issue is debatable. The investigators went -- the Sponsors went over it, but one of the issues is, is it's still considered debatable whether or not high myopia is associated with an increased risk of glaucoma.

DR. WEISS: Okay. So you would like to put as -- if data is gone that four years of specular microscopy, you would like gonioscopy to be done at four years, as well.

DR. COLEMAN: To looking at pigment deposition and increased peripheral anterior synechiae, because those references that Dr. Grimmett found did show that in those eyes that had elevated

pressures that were having problems, they did have increased pigment deposition, and also peripheral anterior synechiae. Glaucoma is a long-term risk for these individuals. I mean, I think that it's something they're going to be living with for a lifetime if they do have an increased risk of glaucoma, because a 40 year old's prevalence of glaucoma is about .18 percent when you look at the Baltimore Eye Survey in Caucasians. And if you do some extrapolations, this could be actually increasing and doubling that prevalence in this age group.

DR. WEISS: Dr. Grimmett.

DR. GRIMMETT: Michael Grimmett. I'm certainly in favor of warning clinicians in the labeling about our concerns about pigment deposition and need for gonioscopy, so that clinicians go ahead and do the correct thing, but the study was approved without gonioscopy. And while I think it's regrettable, I am not in favor of mandating the Sponsor to gather further gonioscopy data. I don't think that would be fair.

DR. WEISS: Dr. Matoba, and then Dr.

Schein.

DR. MATOBA: Okay. I want to ask Dr. Eydelman, when the FDA put this question together, did you want us to just address safety efficacy for each of these refractory subsets, or do you want us to also take into consideration philosophical ideas, such as whether we think that an interocular procedure is justified in a patient who is minus 3?

DR. EYDELMAN: As I tried to explain in my presentation, what I was hoping that the panel will do is look at each of the refractive ranges, and look at the risk benefit analysis for this device, and for other alternative devices for each of these refractive ranges, and make a decision upon that.

DR. WEISS: So with that in mind, let's talk about minus 7 to minus 10.

DR. SCHEIN: So to clarify that, because that is my question.

DR. WEISS: Yeah.

DR. SCHEIN: So the answer is, compared to what? And so the comparison here is not spectacles or contact lenses, it's compared to other refractive --

DR. WEISS: Dr. Rosenthal.

DR. ROSENTHAL: You're not meant to compare it to anything.

DR. SCHEIN: Well, that's not what you said.

MR. ROSENTHAL: You're meant to take the risk benefit ratio of this device.

DR. WEISS: We have the safety and efficacy minus the endothelial cell data for each of these refractive ranges, irregardless of what else is out there. That's what we have to look at. So I'm going to ask --

DR. SCHEIN: That makes no sense whatsoever, does it?

DR. WEISS: But is that what the agency is asking?

DR. SCHEIN: I mean, what -- obviously, it's inappropriate to --

DR. ROSENTHAL: We're asking do you feel a patient with a minus 3 diopter myopia have a interocular lens put in their eye to treat their minus 3 diopter myopia.

DR. MATOBA: That's not the way the question is worded. I thought that's what you were getting at, but that's not the way the question is worded.

DR. ROSENTHAL: And minus 4, and minus 5, and minus 6. So I think maybe we should look at it - is there a range at which you would feel comfortable subjecting a patient with myopia to an interocular procedure in which this device is implanted?

DR. SCHEIN: Okay. So in other words, it is in comparison to other data that --

SPEAKER: No.

MR. ROSENTHAL: Not comparison.

DR. SCHEIN: Not in a quantitative way, but it's --

DR. WEISS: Okay. Dr. Bradley has suggested the following wording, which I think is good wording. If the Sponsor can establish that the endothelial cell count is not declining at dangerous levels, depending on how you want to classify that word, does the panel consider this device safe and efficacious for the following ranges. So let's first

talk about minus 7 to minus 10. If there was no issues with the endothelial cell count data, I'd like a raise -- a show of hands -- Dr. Matoba.

DR. MATOBA: I think risk benefit is different from what you're saying, because safety is never absolute. It's all relative. And so the benefit for a minus 3 is different from a benefit for minus 12 --

DR. WEISS: That's why I'm talking about minus 7 to minus 10 first.

DR. MATOBA: You can't take that phrase out of the question, I don't think.

DR. WEISS: But that's why I'm speaking about minus 7 to minus 10 first. I'd like to clear up those, and then obviously, when we get into the minus 3s, it sounds like it's going to get more contentious. Minus 7 to minus 10, are there any issues that the panel has with safety and efficacy, regardless of --

DR. ROSENTHAL: Excuse me.

DR. WEISS: Yes, Dr. Rosenthal.

DR. ROSENTHAL: I just want to clarify what I was -- a risk benefit analysis, Mrs. Lochner

has told me, does take into account other options. But you are not to compare the option. You are to use a clinical judgment to say whether or not you feel that a certain range would be appropriate for this device.

DR. WEISS: Minus 7 to minus 10, can we have a vote for those who would feel that this is safe and efficacious if the endothelial cell data shows such for minus 7 to minus 10.

(Vote taken.)

DR. WEISS: So we have a majority of the panel who feels it would safe and efficacious for minus 7 to minus 10. Minus 10 to minus 15, can we have a similar vote, with some prompting by Dr. Macsai. That's all right. We'll use you for other votes here, Marian. I'm enlisting you.

(Vote taken.)

DR. WEISS: This is in favor of. So minus 7 to minus 10, and minus 10 to minus 15, it is safe and efficacious. How about minus 6?

SPEAKER: What?

DR. WEISS: I know who I'm dealing with

here.

SPEAKER: Excuse me.

DR. WEISS: Minus 6, how many of you -- I'm not going to go the minus 3 to minus 7 range, because there's going to be possibly a breakdown, so I avoid breakdowns.

SPEAKER: Call a vote.

DR. MACSAI: Can I --

DR. WEISS: Yes, Dr. Macsai.

DR. MACSAI: If we're looking at efficacy and safety, and we have a guidance document that exists for minus 3 to minus 7 for safety and efficacy, and we look at this group, which is how we've broken out minus 3 to minus 7 or 6.9 - I don't remember - compared to the guidance document, okay. You can eliminate the endothelial issue. It meets the criteria, safe and effective.

DR. WEISS: So you would -- you feel for minus 3 to minus 15, it's safe and efficacious. So we can go to minus 3-minus 7. Let's go to minus 3- minus 7. Minus 3-minus 7, can we have a vote by hands for those who feel that this is safe and efficacious.

MS. THORNTON: One, two, three, four, five, six.

DR. WEISS: Hey, it's a good day.

DR. MACSAI: You may not put it in your eye, but it meets the guidance.

DR. BANDEEN-ROCHE: May I just say something for the record?

DR. WEISS: Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: I just want to make clear that I was abstaining because I don't feel like I have the clinical expertise to make the complicated risk benefit decision that you seem to be asking for.

MS. THORNTON: Yeah. Then I'd like to have a negative vote, are there any other abstenders?

DR. WEISS: We're going to have a vote for minus 3 to minus 7, those who did not feel it had evidence of safety and efficacy. Dr. Schein, Dr. Matoba, Dr. Mathers and Dr. Coleman. And then we had one abstention by Dr. Bandeen-Roche.

MS. THORNTON: Okay. I've got it. That's minus 3 to minus 15.

DR. WEISS: Minus 3 to minus 15 at this

point. Are we finished with that question, Question 5. So we're going to go to Question 7 - additional labeling recommendations. What I will do is, interest of time, is mention some of those that have been brought up already, and see if there's consensus or disagreement. There was one comment about adding in the labeling that the stability of the endothelial cell count has not been documented. That might be a moot point if a condition for approval is getting the four year data.

DR. SCHEIN: It's not moot.

DR. MACSAI: It's not moot at all.

DR. SCHEIN: There's still going to be labeling of whatever goes out there. If we approve it with condition of acquiring that data post-approval, then that would have to be in there.

DR. WEISS: Fine. So we'll include that. Dr. Grimmett had indicated white-to-white is not sufficient to determine the lens size. I don't know that that would go into labeling. Dr. Macsai wanted non-Caucasian eyes from the Dominican Republic included. Dr. Coleman.

DR. COLEMAN: Yeah. I wanted to include that long-term risk for glaucoma are unknown, and then to also in the table that they have on page 20 of 25, they have glaucoma there too. And I would change that to elevated interocular pressure, ocular hypertension, whatever definition they use. And also, for the interocular pressure greater than 25 or greater than 10 --

DR. WEISS: Can you --

DR. COLEMAN: Slow down.

DR. WEISS: Slow down a little.

DR. COLEMAN: I have one, and I think that that's misleading because they had five patients that had pressures of greater than 25, or greater than 10 millimeter increase during baseline to 36 months. And so I think it's misleading just to use that last visit, because pressure does vary, and we don't just use one --

DR. WEISS: So tell me what you want.

DR. COLEMAN: So I want IOP greater than 25, or greater than 10 increased from pre-op. And I want the exact number, which is 5, instead of 1. And

so that would be a percentage of 1.4 percent instead of 0.2 percent. This is in table --

DR. WEISS: I'm going to actually need you to write this down, because it's going too quick for me.

DR. COLEMAN: Okay.

DR. WEISS: Dr. Macsai had included data about halos and wanted to include data about patients having complaints of halos and glare.

DR. MACSAI: Can I elaborate?

DR. WEISS: Okay. Yes, Dr. Macsai.

DR. MACSAI: I also wanted to include limbal pathology as an exclusion criterion. I mean, the same as a pterygium, you can't measure white-to-white.

DR. WEISS: I'm just wondering if the Sponsor had any patients with pterygias or things along --

DR. EDYLMAN: I think in general, most of those ociopathology was excluded.

DR. WEISS: Okay. So that's fine. Dr. Grimmett had suggested having something in labeling

about a learning curve, that there's a learning curve of the surgeon with a higher rate of upside down lenses and cataracts, and surgeons with less experience.

Dr. Macsai had also requested, and I don't know -- this may not go on labeling, but had requested that the 65 excluded eyes was -- if you could elaborate on that.

DR. MACSAI: Sixty-five eyes with pre-existing conditions were included in the study. It would be nice to know what were the pre- existing conditions, what happened to those patients. It would give the implanting surgeon and patient tremendous information, so let us know what happened. What were the pre-existing conditions, and what happened to those patients?

DR. EYDELMAN: There was actually a section in the PMA that talked about that.

DR. MACSAI: Oh, I missed it. Sorry. We'll include it then.

DR. WEISS: So we don't have to get involved in that then.

MS. THORNTON: You want that included in the labeling?

DR. MACSAI: Yeah, in the surgeon's information.

MS. THORNTON: Okay.

DR. WEISS: Dr. Schein, Dr. Matoba, and then Dr. Bradley.

DR. SCHEIN: I would like to see the more severe complication rates reported on a per-patient basis, rather than on a per-eye basis.

DR. MATOBA: Under patient precautions, pigment dispersion should be listed.

DR. MACSAI: Can you talk a little louder?

DR. MATOBA: Yes. Under patient precautions or relative -- yeah, under patient precautions, I would like pigment dispersion to be listed. I don't think it is right now. And on page - let's see - L-36, which is the beginning of the patient information draft, the third paragraph where they mentioned the term "phakic interocular lens surgery", I don't think that the average patient knows what phakic means. That term should be explained. It

never comes up again as you go on reading it. It should be explained, and I think there should be a clearer discussion of the alternative treatments for myopia.

And then lastly, on page L-43, "List of Adverse Events and Complications", I think they should -- even though it was not observed in the study, I think they should mention the possibility of endophthalmitis and loss of the eye, even though it's very rare, but that's risk with interocular surgery.

DR. WEISS: Dr. Ho, and then Dr. McMahon.

DR. HO: Allen Ho. I would propose that the labeling include the increased risk of vision loss from retinal detachment remains unknown.

DR. WEISS: Well, the risk, not the increased risk.

DR. HO: Yes, I'm sorry. The risk.

DR. WEISS: Dr. Bradley, then Dr. Sugar, then Dr. Bandeen-Roche.

DR. MACSAI: You missed McMahon.

DR. WEISS: Dr. McMahon. Excuse me.

DR. McMAHON: I'd like to bring up a

completely new issue, and that is, I have a problem with the name of this device. This device has nothing to do with a contact lens, and I think it is a disservice to the public by using this term. I think it's a Euthanism probably from the marketing department gone hog wild. And I would like to see all mention to this in the device and labeling removed.

DR. MACSAI: What?

DR. McMAHON: The word "contact lens" I want removed from the name and all labeling.

DR. WEISS: Doctor -- Sally. Sorry.

MS. THORNTON: I'm Dr. Sally.

(Laughter.)

DR. WEISS: AT this point, I'll give out free M.D.s just --

MS. THORNTON: It sounded like part with Dr. Phil and Dr. Ruth.

DR. WEISS: Your book comes out soon.

MS. THORNTON: I also think we need to get some comments on the labeling from the consumer representative.

MS. SUCH: Now?

DR. WEISS: Now is as good a time as any.

MS. SUCH: Okay.

MS. THORNTON: Before we leave this subject.

MS. SUCH: Good. Glenda Such. A couple of things. One is, I could ask a question first and that is, precautions -- excuse me. On the precautions versus the contraindications, there's a mention about -- we have just brought up also about retinal detachment. And I wonder if there shouldn't be something in the contraindications about retinal detachment. How long after retinal detachment should you not have this process? That actually should be in there.

Also - I just went blank.

DR. WEISS: I believe it was an absolute contraindication for inclusion into the study, so we don't -- we won't change that. And that would be up to an individual physician if they intended to use this in --

DR. MACSAI: It's not a contraindication.

DR. WEISS: A retinal detachment is not a

contraindication?

DR. MACSAI: No.

DR. HO: Correct. The definition was stable retinal exam, so that -- you can have a very stable retinal exam post retinal detachment, and in fact, after a retinal detachment surgery, you may be at less risk for a problem, i.e., retinal detachment if you have it, so I'm comfortable with that. To answer your question, Glenda, I would say -- I would leave that to surgeon discretion really.

MS. SUCH: And not have it in the patient --

DR. HO: Not have a specific time frame.

MS. SUCH: Okay. I was just concerned about that. The other is something that's very small housecleaning part. It's on the same issue as the phakic, and that is talking about in the very beginning of the patient brochure, they talk about that it's 3-D to 20-D before they get into what a diopter is. And let me tell you, most people wouldn't know a diopter from a hole in the wall, so that should be spot up right away. And even though there's a

mention about that there's a glossary, most patients won't look at the glossary unless they really, really a very, very academic minded, so anywhere you can, to write out the actual words, even though I know it's going to add to printing cost to actually write out the words. That's the majority I have right now, this very moment.

DR. WEISS: Just in terms of the patient information, I had -- looking at the labeling, I think it should be listed in patient information that the higher myopes should not expect the same results as low myopes, because this reduces, does not correct myopia. I'd like long term effect on the endothelium is not known. And in mentioning - sort of following up on Dr. McMahon's comment - in the glossary, there's a definition, Collamer ICL is a collagen-based contact lens. I have to say, that's the name of this device, but if I -- I think the average person, if they see Collagen-based contact lens, that certainly invokes something different than an interocular lens, which we're discussing. I'm not sure how to address that issue, but Dr. Bradley will

tell me.

DR. BRADLEY: Yeah, two points. One, on the issue of naming, I agree with Dr. McMahon. I think calling this a contact lens will be grossly misleading to the public. They already have a sense of what a contact lens is. It's well-defined. This is not a contact lens. It never will be a contact lens, and to tell the public that it is, I think is misleading. So perhaps we could take a vote on that, if there's some contention over that.

Second issue, in spite of what Dr. Schallhorn assured us this morning, the issue of pupil size still concerns me with this product. I mean, it has a small optical zone. An optical zone size that would not be considered safe for standard refractive surgery. And even with the larger optical zones used in current LASIK, we're still concerned that the procedure might not be appropriate for people with very large pupils. And I wonder if some labeling for this particular device should also warn the physician and the patient that if they happen to have large pupils, this device may cause them problems at night.

DR. WEISS: Well, I think what would be more accurate to say is the effect of pupil size is not known, because we have no evidence that it does or doesn't. Sally has pointed out to me, I could see the National Enquirer headline saying I got endophthalmitis from my contact lens. Those weren't her exact words, but distancing herself from my comments already, didn't take long. Dr. Coleman, Dr. Grimmett.

DR. COLEMAN: So for patient labeling issues, I also wanted to recommend, concerning putting in that they may need to use medications chronically to control eye pressure, because a lot of the patients had -- they had like -- they have so far two patients that have needed to use topical beta blockers chronically for their ocular hypertension.

DR. WEISS: Well, wouldn't it be more fair to say glaucoma is a risk, than to tell you what the treatment is going to be?

DR. COLEMAN: They haven't shown that you've gotten glaucoma. They're just describing that you've gotten high eye pressures. And according to

them, they didn't have glaucoma. They just -- that's why I wanted to change that labeling, because the risk of glaucoma is unknown. They weren't really -- they aren't doing visual fields, and you don't see anything about the optic nerve. And so you really can't say anything about glaucoma. They aren't doing angle evaluations. I mean, they aren't doing a glaucoma evaluation, so they really --

DR. WEISS: Okay. The agency will describe it.

DR. COLEMAN: Yeah.

DR. WEISS: Okay. Any other -- yes. Go ahead.

MR. CROMPTON: Just a little fair balance from the industry rep on labeling, is FDA really does work closely with the Sponsors on labeling. And a lot of the comments that I'm hearing, these kind of generic comments that aren't specific to the study here, really can be addressed in precautions, black box warnings, things like that. And I know that all companies want to represent the product correctly.

When we get into trade names of products,

that is a matter of some concern to companies and the agency. And I think the agency guides that, rather than the panels. So trade names get into patent issues, copyright, all that sort of stuff. As long as claims are not being misrepresented, I think that is a key thing.

DR. WEISS: The only problem is that contact lens is --

MR. CROMPTON: I understand the issue.

DR. WEISS: I would say that's somewhat deceptive.

MR. CROMPTON: I understand the issue, and I think FDA has a lot of practice dealing with companies in terms of how they name their products.

DR. WEISS: Ralph, do we need -- does the panel need to get involved in this issue, or does not?

DR. ROSENTHAL: (Nodding head no.)

DR. WEISS: Fine. I had two things on the physician labeling. Is on page 6, there's a discussion of calculation of lens power. I'd ask the panel and the agency, should they be specifying the two formulas that they specifically used in this

study, or just say calculation of lens power? Do you think it would be helpful to specify the formulas that they used, or not really? Anyone. Dr. Sugar. No, just leave it as is.

Page 14, they indicate the post-op regime should be Ocuflox and Tobradex. I don't think that it has to be specifically -- there's no reason why they have to use those particular drugs. And I think that could read that the post-op regime used in the PMA were those drugs. Does anyone disagree with that? No? Any other labeling?

DR. GRIMMETT: I have a question.

DR. WEISS: Yes, Dr. Grimmett.

DR. GRIMMETT: Is the agency going to obtain stratified data by lens optic size on the symptom data, the halos and stuff? Yes. Okay. Moot point.

DR. MACSAI: That's what I asked for.

DR. GRIMMETT: I just want to make sure it's stratified.

DR. WEISS: Does anyone want to have any warning in there that 20 percent of patients fell out

of the usual endothelial cell loss, and had a higher rate of endothelial cell loss? Dr. Schein.

DR. SCHEIN: I think the most direct thing to do is simply to show some data at a level that the people reading this would understand. Maybe a histogram of cell counts at baseline and at 3 or 4 years.

DR. WEISS: Dr. McMahon has pointed out to me that there's a -- I have one list of questions, and he has another. And on his other, a very important question that has been not handled by panel at this point, so I'm going to jump around. It is, do the safety and efficacy data for eyes with pre-operative myopia of greater than 15 to 20 support approval in this refractive range? We've gone up to 15.

MS. THORNTON: We voted on that.

DR. ROSENTHAL: You just did efficacy. I would like to hear your discussion on safety issues, other than endothelial cell counts, which you're addressing globally.

DR. WEISS: Above 15. We've gone up to 15, but we omitted above 15 to 20. Those had a higher

rate of loss of best corrected vision. I think we -- we did talk -- what do you specifically want us to address, because I have highlighted that the panel did say it was efficacious for reduction of myopia over minus 15.

DR. ROSENTHAL: The other safety issues.

DR. WEISS: The other safety -- is the panel satisfied with the safety profile, aside from endothelial cell counts, in this group of higher myopes? Dr. McMahon.

DR. McMAHON: I have some concerns in that in almost all categories, there's a higher incidence of troubles, if you're looking at the troublesome categories, and the numbers are relatively small. I think it was 57 eyes, and so I have my concerns about that. And actually would like to see either more data to expand the range to 15 to 20 that demonstrates an acceptable safety profile, or to exclude it.

DR. WEISS: Does anyone else have any concerns? Dr. Mathers, then Dr. Coleman.

DR. MATHERS: But I think in this particular group, this device has a very, very strong

appeal, because there is nothing else that can help these people besides a contact lens, so in the risk benefit ratio, I think that this is -- it's my own opinion that this actually has the best risk benefit ratio of any of the other degrees of myopia, because nothing else is available.

DR. WEISS: I apologize. As I recall, I think 100 percent of people in that group would have it done again, so even though the satisfaction wasn't the highest, they had the highest rate of deciding they made the proper decision, probably particularly for the reason that you mentioned, that if you have a majority of those people ending up 20/40, that's probably a miraculous result for them.

DR. MATHERS: The alternative treatment is clear lens extraction, and this is preferable.

DR. WEISS: Dr. Coleman, then Dr. Ho, then Dr. Bradley.

DR. COLEMAN: Yeah. I just wanted to point out that in this group, the incidence of pressures greater than 10 millimeters of mercury over from baseline was greater. It's about 4 percent

versus the 1.4 percent.

DR. WEISS: So, I mean, that could be -- and this is separate, and I apologize for digressing, but it probably -- I mentioned putting in the patient information that the high myopes didn't have the same level of efficacy, and we should also probably indicate they had a higher level of risk at the same time. Dr. Ho.

DR. HO: Yeah. Dr. Mathers makes a very good point. The issue here for those 28 eyes that were over 15 diopters is -- I'm, you know, very concerned about the possibility of retinal detachment with any kind of procedure in those large myopic eyes. But if you look at those that are willing to do it again, it's very telling. I think it was, as you mentioned, zero out of 28 were not willing to do it again. And the point of the other procedure being clear lens extraction, I think potentially could be fraught with more risk. And that's why I'm supportive for this group.

DR. SCHEIN: Jayne.

DR. WEISS: Dr. Schein.

DR. SCHEIN: This could be dealt with in labeling by simply saying this is the highest risk group. Notice, one of the people that wanted to have it again had a macular detachment, isn't seeing very well. Now how do you interpret that?

DR. WEISS: Hope springs eternal. Dr. Bradley.

DR. BRADLEY: Just to clarify a point Dr. Mathers made. I think you perhaps meant to say these people have no other surgical options. They clearly have other options.

DR. MATHERS: Contact lens, and spectacles.

DR. WEISS: You get terrible vision though.

DR. BRADLEY: They don't work very well.

DR. MATHERS: But yes, it's something.

DR. WEISS: Dr. Bandeen-Roche.

DR. BANDEEN-ROCHE: Would someone briefly speak to the clinical significance of the trace anterior subcapsular, so in other words, between those and the nuclear cataracts, there were 13.5 percent in

this group who had a cataract of some type. And is that an acceptable trade-off?

DR. WEISS: Dr. Eydelman, can you speak to that?

DR. EYDELMAN: The slide is up.

DR. WEISS: Okay. Great. Well, you know, we are speaking though a very small number of eyes.

DR. EYDELMAN: Thirty-one.

SPEAKER: They're at risk for cataract in any case.

DR. WEISS: I'm not sure what conclusions can be reached on that small number.

DR. MACSAI: They're at a greater risk for nuclear sclerotic cataract.

DR. WEISS: Dr. Macsai.

DR. MACSAI: Oh, sorry. Dr. Macsai. These patients are at greater risk for nuclear sclerotic cataracts at an earlier age, whether or not they have this implant -- this device implanted.

DR. WEISS: So I would suggest that this could be handled in -- the sentiment I'm getting is that there aren't a lot of good options, that even

though the safety and efficacy were not as good as other ranges, this could be addressed in labeling to let the patients know that their expectations should be less. I see some nodding by the panel, so that will be good enough for me.

And we already indicated that we wanted this to be listed as reduction of myopia, as opposed to correction. Dr. Sugar had mentioned a couple of other things. There is something in patient and physician labeling, indicating that this device improves the quality of vision. I think you mentioned reduction as opposed to correction, if we're talking about contrast sensitivity or rather than just saying the quality of vision. Am I correct on that, Joel?

DR. SUGAR: Well, I can't speak to why the Sponsor put it in there, but they did, I think, ask the patients about their quality of vision. I don't think that's sufficient. I think you could say it may improve the quality of vision, but then they should put the data in.

DR. WEISS: And then you wanted a brochure with a picture of the device and the positioning.

Anything else in the labeling? I think we answered above 15 to 20. Dr. Grimmett.

DR. GRIMMETT: Let's take a vote on it.

DR. WEISS: I don't -- I mean, unless you want to vote, Ralph? Fine. Above minus 15 to minus 20, excluding endothelial cell data, who would agree that this shows safety and efficacy?

(Vote taken.)

MS. THORNTON: Six for.

DR. WEISS: Six for, and who would --

DR. ROSENTHAL: Four there, three there - that is seven.

MS. THORNTON: Well, why don't you count. I can -- one, two, three, four, five, six, seven. You're right. Seven for.

DR. WEISS: And those would disagree with safety and efficacy, please raise your hand.

MS. THORNTON: Two against.

DR. SCHEIN: There's this problem that I would vote for approval, but I don't think it's particularly safe.

DR. WEISS: Well, it's both. It's a

marriage, safe and efficacious.

DR. SCHEIN: Yeah, that's the problem.

DR. WEISS: So life is full of -- so would you vote for -- with those two, safe and efficacious, would you vote for approval or not?

DR. SCHEIN: Presuming all the information is in the labeling, I would vote for approval.

DR. WEISS: Okay. Fine. Eight-one. Any other labeling issues? Okay. Seeing no other labeling issues, does the FDA have any other questions that they want the panel to address?

MS. THORNTON: Last chance.

DR. WEISS: Last chance. Okay. Seeing no other questions, then we are going to go to our open public hearing. And seeing no one for the open public hearing, we will now move on from that. I hear applause, so that might have been the correct decision. FDA closing comments. No closing comments. I think everyone has been beaten into submission. Sponsor closing comments. Ah, FDA closing comments.

DR. CALOGERO: Yes. Hi there, Don Calogero. I'd like to clarify something. I think

there's a little sort of confusion here in terms of these rates. And we were throwing out rates, Dr. Macsai threw out rates, 1.8 percent, ANSI is 2 percent, the panel gave a rate of 1.5 percent, all in the same ball park. But the rate that you threw out, 1.8 percent and Gerry calculated 2 percent, those are mean rates. The rates from ANSI and the rates from that panel discussion are the upper 90 percent confidence intervals. So in terms of ANSI and that discussion, the upper 90 percent confidence interval needs to be below that point.

If you look at the upper 90 percent confidence interval of the data out to three years, it's actually about 3-1/2 percent. So you're saying 3-1/2 percent, then is acceptable. If you look at the Sponsor's data, from year 3 to year 4, at the upper 90 percent confidence interval, they have met that criteria of 1.5. It's 1.42 or something.

The only problem that I hear from the discussion about that data is, it may -- that group may not be representative of the entire population. You may sort of a sampling bias or something, so I

just want to point out that there's sort of a little miscommunication here, or confusion. The actual rates that the Sponsor has from year -- three months to three years are very different than the levels that ANSI has, and ISO has, and was recommended previously by the panel, so I just wanted to clear that up.

DR. GRIMMETT: Thank you.

DR. WEISS: Sponsor closing comments.

DR. SLADE: The battery on our laptop is not up to the length of your discussion.

DR. WEISS: That comforts me, Dr. Slade.

MS. THORNTON: Do you want the projector on?

DR. SLADE: Yes. We would like the projector on. I really appreciate you all staying to listen to my talk. Okay. There. Okay. And what I would like to do is give you our closing comments from the Sponsor. Excuse me just a minute. This is not actually my computer. Is the toggle F10? F8. Okay. Super.

Let's just go right to the chase to our comments. What do we know, and what do we not know

about this PMA and this device? What are the current standards of requirements for safety of the corneal endothelium for any device? And what do we know about endothelial safety for this particular device? What information do we have to support a determination of reasonable assurance with post-market labeling and follow-up, a reasonable assurance of safety today, and how do we best add to the evolving knowledge-base in this area over time, a needed area, a needed area for our patients.

We've looked at the standards for endothelial cell safety. The ANSI standards of 1-1/2 percent. You add the .6 percent, somewhere around 2 percent, and we don't have any targets for hexagonality, or coefficient of variation, although we've seen that those can be the most sensitive indicators of endothelial stress. That's what we know is the standard.

Endothelial safety with the ICL, we have a cumulative total mean loss of 8.4 to 9.7 percent. We do have suggestion of endothelial cell stabilization, or a leveling of cell loss between 3 to

4 years. We have it with two different cohorts, the 57 eye cohort, and the 37. While those aren't our largest numbers, those are our best models. The 37, for example, are the people who made every single visit, so it's the best models, and we can certainly post- marketly follow that particular cohort up.

And then in addition to that, in addition to that, we have the percent hexagonality and the coefficient of variation data, which easily supports the absence of chronic endothelial stress. This is that 37 eye cohort I just mentioned. And if anything, it's trending to a leveling-out, or certainly no farther down.

It's important to look at these again. This is the percent of hexagonal cells. Anything over 45 percent is a winner, and this is clearly, throughout the entire follow-up, over that, and it's stable. It's not dancing around.

The coefficient of variation is the same thing. Anything that is not above 45 is, again, a winner. And this does fit into that to the adequate confidence intervals, and it's stable. It's stable

over time, just like the visual acuity results, just like the refractive stability that I showed you.

Further, if you're trying to figure out the safety of this lens, I would challenge you to postulate a clear mechanism for chronic endothelial cell loss due to the clinical procedure, which is cataract surgery with a lot of the steps left out, or the ICL, the material itself, which is a proven approved material behind the iris. We have no evidence of inflammation over time when assessed with the most sensitive methods we have today. Don Sanders, I think, made that point clear. And we have no evidence of corneal stress or instability based upon the most sensitive measures of morphology by I think who we -- the person, Henry Edelhauser, who we all respect, over time. Again, you've seen the morphology of endothelial cells. If we look at the cell flare study, at no point in time did we ever get the cohort outside the normal range. That's significant.

Further, I think we should stress again what Hank Edelhauser presented to us. There's a

change. We're learning about our understanding of the corneal endothelium. There does appear to be a reservoir of endothelial cells in the corneal periphery, based upon his lab, and earlier confirmatory studies. There's even the good evidence for peripheral corneal endothelial stem cells, even in adult corneal tissue. And again, Dr. Edelhauser, I think, has well-documented this, just the simple references, the fact of increasing cells. And then when we make our incision into the cornea, we're not even approaching where we have most of these safety cells, which is superior.

Further, our understanding of the corneal endothelium, I think we've all struggled today. And if anything, it's proven that a linear modeling of endothelial cell loss over time is difficult based upon our current knowledge-base. The non-homogenate endothelial cell density, the presence of an endothelial cell reserve in the periphery, including the stem cells, and the potential for these cells to migrate from the higher density periphery to the lower density central endothelium further supports

reasonable safety for this device.

From Dr. Edelhauser, the higher endothelial cell density found in the paracentral and peripheral cornea affords an additional reassurance of safety beyond the morphology for the endothelium in patients implanted with the ICL. The surgical incision for the ICL is corneal, and temporal, and it's at a distance, and it's only a couple of clock hours away from the largest endothelial reserves which reside in the superior corneal.

So to finish this out, what do we know today? And we actually know, I think, a fairly good deal. Well, we realized, and we continue to realize the need for additional options, additional good clinical options in refractive surgery. And one note about this - the beauty of this is it's a non-dose dependent procedure. LASIK, the more LASIK you do, the more trouble you run into. This is the same procedure, the same lens, whether it's a minus 3 or minus 15, or a minus 20.

Endothelial morphology represents a highly sensitive measure or indicator of corneal endothelial

stability, and I think we've seen the results, seen the studies that back that up. And in the ICL population, I don't know how the results could be any better. It clearly indicates a stable endothelium without stress by morphology.

We believe the stabilization of endothelial cell loss occurs between three to four years. We have the absence of any cases of corneal decompensation in ten years of history greater than 30,000 implants internationally. Again, as I mentioned, I don't know if we got all of the data from those patients, but I do believe that the first person that had a corneal decompensation would be quite - - we'd know about that.

There is a iron-clad Sponsor commitment to continued specular microscopy data. I don't have a financial interest in STAAR. I wasn't an investigator in this study. I am a paid consultant, but I can assure you of their commitment to continue the collection of specular microscopy data post-market approval, in all study patients through five years or beyond with the same rigor of analysis, the same lab,

the same Dr. Edelhauser looking at the specular microscopy images.

So a long-term commitment to surveillance of study patients for all safety findings. A well-developed training program. Now we've had the -- you know, is this something that only the creme de la creme surgeons can do? Well, remember when LASIK came along and everybody would say well gee, that's pretty crazy. You know, only corneal surgeons should be doing that. And it just didn't pan out that way.

I would submit to you that that was a procedure where surgeons had to learn new steps. This, they don't. It's all cataract steps. I do believe strongly, having been involved in directing the LASIK courses, that the training program will be excellent and superlative beyond what we've had before. And finally, the Sponsor is totally committed to labeling to encompass your recommendations, no matter how many volumes, or how the package insert becomes. And that to the panel and the FDA, to provide further assurance of safe use of the ICL.

I submit to you that the clinical data

presented in the PMA does establish the effectiveness of the myopic ICL for the correction or reduction, as labeling -- as we are dictated to by you for labeling, between minus 3 and minus 20. And I submit to you that the clinical outcomes presented in this PMA provide a reasonable assurance of safety of the myopic ICL in this patient population, this study designed for moderate to high myopia. Thank you very much.

DR. WEISS: Thank you very much, Dr. Slade. I would like to thank the Sponsor for an excellent presentation, the primary reviewers, and the member of the panel, as well as the agency for the usual detailed evaluation of the data, and now we will move to the voting options, which will be read by Sally Thornton.

MS. THORNTON: "The Medical Device Amendments to the Federal Food, Drug and Cosmetic Act as amended by the Safe Medical Devices Act of 1990 allows the Food and Drug Administration to obtain a recommendation from an expert advisory panel on designated medical device pre-market approval applications that are filed with the agency. The PMA

must stand on its own merits, and your recommendation must be supported by safety and effectiveness data in the application, or by applicable publicly available information.

Safety is defined in the Act as reasonable assurance based on valid scientific evidence that the probable benefits to health under conditions on intended use outweigh any probable risk. Effectiveness is defined as reasonable assurance that in a significant portion of the population, the use of the device for its intended use is in conditions of approval when labeled will provide clinically significant results.

Your recommendation options for the vote are as follows. Number one, approval, if there are no conditions attached. Number two, approvable with conditions. The panel may recommend that the PMA be found approvable, subject to specified conditions, such as position or patient education, labeling changes or a further analysis of existing data. Prior to voting, all of the conditions should be discussed by the panel. Not-approvable. The panel may

recommend that the PMA is not approvable if the data do not provide a reasonable assurance that the device is safe, or if a reasonable assurance has not been given, that the device is effective under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

Following the voting, the Chair will ask each panel member to present a brief statement outlining the reasons for their vote." Thank you. Jayne.

DR. WEISS: Thank you. I'd like to have someone make a motion. Dr. Sugar.

DR. SUGAR: I'd like to move approval with conditions with the volumes of conditions that Steve Slade mentioned.

DR. WEISS: Well, one of the --

MS. THORNTON: Well, you can't do that.

DR. SUGAR: I know, but Jayne has them all listed on her computer, and she can give us the words.

DR. WEISS: Okay. Do we have a second for approval with conditions? Dr. Mathers and Dr. Macsai second it. There were two conditions, there was a

choice of one condition that I think we do need to have the panel list. We will, of course, vote on the secondary motions, the conditions, before we vote on the primary motion. But the secondary motion, as far as data to be included for specular microscopy and when that would be needed - I need someone to phrase that for me, because there was a disagreement among the panel, and I need that to be included here.

MS. THORNTON: Are you calling for a condition now?

DR. SUGAR: Yes.

DR. WEISS: What is your --

DR. SUGAR: With the condition that after approval, data continue to be acquired on endothelial cell density on an annual basis, up to a minimum of five years.

MS. THORNTON: Is there a second?

(Seconded.)

DR. WEISS: So there's a second for the -- and can you repeat that condition, Dr. Sugar, because what -- if it's all right with agency, before we go on with additional --

MS. THORNTON: We can discuss it after the second.

DR. WEISS: Okay. Can you repeat what that motion is and then we're going to have discussion of that. And the a vote of that condition.

DR. SUGAR: Approvable with conditions. One of the conditions being that data continue to be acquired on an annual basis on endothelial cell density to at least five years.

DR. WEISS: Can you --

DR. GRIMMETT: For clarification, he's recommending approval now, post-market later.

DR. ROSENTHAL: Approval now, and the endothelial cell data will be collected after the approval --

DR. SUGAR: Correct.

DR. ROSENTHAL: -- for four and five years. And longer, if need be.

DR. WEISS: Okay. So approval now, and I would like the panel to be extremely clear when they vote on this. This is approval now, and then the endothelial cell count data will be collected

afterwards, after approval. We will have a discussion, and Dr. Bradley will have the first point. After we have discussion of this secondary motion, we will vote on the secondary motion before we go on to other labeling. Dr. Bradley.

DR. BRADLEY: I thought in our earlier discussions that approval was going to be conditional upon the four year data convincing us that, in fact, endothelial count decline was not at a dangerous level.

DR. GRIMMETT: Then vote against this motion.

DR. WEISS: This is why I wanted a particular motion put forward for a vote. If you disagree with this, as Dr. Grimmett so kindly pointed out, then you vote that you disagree. And if you agree with it, then you vote that you agree. Is there any discussion, aside from when you disagree you vote no, and when you agree you vote yes. I assume not, so Dr. Ho.

DR. HO: Allen Ho. I would like to add to that, as part of discussion, that the annualized rates

of retinal detachment be included.

DR. WEISS: This is separate. That's a separate condition. This is not, as Dr. Slade indicated, we will have a volume coming up. But hopefully, it will be done shortly enough. This is just this particular point. Dr. Bradley.

DR. BRADLEY: A question -- the motion is that the data be collected post approval.

DR. SUGAR: That's correct.

DR. BRADLEY: Do you have any desire that something specific be done with the data once collected, or is that irrelevant to your motion?

DR. SUGAR: It's certainly not irrelevant. I don't know how specific we need to be with that, but the data be reviewed by the agency and apropos of our discussion, if the endothelial cell density continues to decline at the same rate, that the issue be represented either to the panel, or that there be some further discussion about whether approval should be continued.

DR. WEISS: Just for clarification, Ralph, what would the -- aside from the statement that Dr.

Sugar just made as far as collecting the data, do you need any further clarification at this point from the panel what we mean by collecting the data, what we want you to do with the data, or that would be sufficient for you at this point?

DR. ROSENTHAL: I think we understand the mood of the motion.

DR. WEISS: Okay. The mood --

DR. ROSENTHAL: The question is, and I'm not sure I can give you an answer, is if the endothelial cell count continued to drop at 4 and 5 years, I'm not sure what our options would be. And that is something we would have to take up with higher order people in the agency.**

DR. SUGAR: Well, could not rescind approval?

DR. MACSAI: Recall? I mean, is that not an option? You've done it before.

DR. ROSENTHAL: Everything you've said are options.

DR. WEISS: Would we need to -- would Dr. Sugar need to amend his motion to include what his

desire for -- he would not. Dr. Sugar, is there anything else you wanted to add to that motion? Are you satisfied --

DR. ROSENTHAL: I just wanted to add, that I've just been informed that a PMA has never been withdrawn from --

DR. SUGAR: You mean approval has never been withdrawn.

DR. ROSENTHAL: Approval has never been withdrawn. There could be the issue of generalized recall. I'm not sure how that would work. I've never had it. Oh, I have had one. It's not easy, based on endothelial cell counts. And on 4 and 5 year data when you're looking at data, possibly 20 years down the line.

DR. WEISS: I assume the intent of Dr. Sugar's motion was to -- because he believes there's reasonable safety and efficacy, but he would like to be assured of that. And if there was any evidence to the contrary, that the agency could act on that evidence to the contrary. What I'm hearing from you now is that the agency would have difficulty acting on

that evidence.

DR. ROSENTHAL: We would have difficulty withdrawing the PMA. It's never been done, and you can -- I think you can probably sense the problems we would have in dealing with a company that has four and five year data that shows a 1.9 percent drop in endothelial cell counts, with no corneal edema, and no problems. And we're saying well, it should be recalled because 20 years from now, patients could get in trouble. I mean, I just don't know where that argument could go, and I'm sure it would not stop at me.

DR. WEISS: Is there any way that the motion could be amended to have the end result that Dr. Sugar is looking for, in that if there is a concern about safety, then there could be a recall?

DR. ROSENTHAL: No.

DR. WEISS: So then from what you're telling me, it's pointless to get any data afterwards, since there's nothing you can do about it.

DR. SCHEIN: How about labeling changing?

DR. WEISS: Dr. Matoba.

DR. MATOBA: Dr. Schein said a labeling change could be made.

DR. WEISS: So a labeling change could be made, but the device would still be on the market. Dr. Mathers, and then Mr. Crompton.

DR. MATHERS: The collection of this data is important clinically. I mean, just because the device is out there, doesn't mean that surgeons have to put it in. If they have a clear and overwhelming indication of a risk, then it -- and that data is collected because we are telling them to do it, so then it will help the public to know that.

DR. WEISS: And I would be -- I would assume this data is not confidential. Is this data confidential? This data is not confidential, so it would be released for public information?

DR. ROSENTHAL: Once the PMA is approved, the data that comes in subsequently would become part of the new -- I mean, it would come in as an amendment, and we would amend the safety -- the summary of safety and effectiveness. And we would amend the labeling.

DR. WEISS: So it is not confidential. It would go into labeling. The lens -- if there were any issues, the lens would not get recalled. PMA would not be rescinded, but that it would go into labeling, and it would be out there for the public. Yes.

MS. LOCHNER: Yeah. And just for the record, I want to make clear, the FDA does have the authority to withdraw approval of the PMA. However, we do want to caution you that this is an extremely high regulatory burden to meet. And, in fact, it has never been done in the device center because of that high legal and regulatory burden that we have to meet to withdraw the approval. And I think, frankly, it would be very, very difficult for an ophthalmic device. So what we can do is other things, such as push for a mandatory recall of the product, or other authorities. Ask the company to voluntarily withdraw the PMA.

There are other things we can do, but -- and certainly, things like mandatory recall, that assumes a certain acceptance by the company and agreement that there is a problem, so I just don't

want the record to reflect that there's nothing FDA can do once a PMA is approved. We can withdraw approval of the PMA. It's an extremely high legal and regulatory burden, however.

DR. WEISS: Mr. Crompton.

MR. CROMPTON: And I would thank FDA for that comment. FDA has a variety of enforcement tools, as we know. And companies are not in the business of putting unsafe products on the market. There's no vested interest for a company to put on a product that is showing a safety profile that is not being reflected in terms of accurate labeling and communication to potential surgeons that are using the device.

I would comment though, that this is in the danger of statistics and extrapolation, that this is a challenge, I recognize. We had a recognized expert here today who could not tell us what the rate of endothelial cell loss is. To hold a Sponsor to that standard is almost unprecedented for a device, for them to do that sort of basic research. Unusual for me to see that the panel is unanimous saying that

we have an effective treatment here, and frankly, a reasonable safety profile for this device. That word "reasonable" means something, and Dr. Rosenthal gave an excellent, excellent definition of what the Act requires for reasonable evidence of safety.

I think the Sponsor demonstrated that today. The post-market scenario is real. This company is committed to doing that. FDA will look at that data on an annual basis. And believe me, if the safety profile isn't there, there will be a discussion with the company. We just know that in the industry. So I can't advocate on the part of the company, but in terms of the industry position, we cannot be put on to answer these basic scientific questions when we bring new devices to the market.

We deal with protocols that were actually blessed by the agency over five years ago, and now other things are coming up as we gain experience with these devices and with new treatments. A factor, unfortunately, that you cannot consider in your deliberations, but needs to be put up there, because it's been put up four times today. You've got over

30,000 implants in Europe with a 10 year history. If there was a problem with corneal edema, I think the company might know about that.

DR. WEISS: I don't think -- actually, from what I hear from the panel, no one is really worried about corneal edema. As Dr. Mathers has indicated, he just wants people to have 1500 cells at the time of their demise. A good goal for all of us, I will mention.

Any other comments on this motion? Otherwise, we'll put it to a vote. If there are no other comments, I just want to clarify what's been said, is that this data would be obtained after this device is released to be used. It would be difficult, although not impossible, for the FDA to act on any adverse information coming in from that data. Am I -- Dr. Rosenthal, anything else you'd want to add for my interpretation? If not, if everyone understands this motion, then I would like those in favor of the motion -- perhaps, Dr. Sugar, could you just restate the motion, and then I'll -- you can't restate it. Okay. In that case, no restatement of the motion. We'll

just have a vote on it from your memory.

MS. THORNTON: Would you please try to state it.

DR. WEISS: Okay. I -- would I try to state it? I've stated it enough. Joel, please, have some pity.

DR. SUGAR: Yeah. I don't think this motion will pass, but I'd like to move for --

DR. WEISS: I'd move to strike that one from the record.

DR. SUGAR: One of the conditions being that with -- that post- approval data be acquired on endothelial cell density on an annual basis up to at least five years.

DR. WEISS: Fine. All of those in favor of the motion, please signify by raising your hand.

(Vote taken.)

DR. WEISS: All of those who are against, signify by raising your hands.

(Vote taken.)

DR. WEISS: Any abstentions on this? So the motion passed 6-5. Dr. Sugar.

DR. SUGAR: I'm surprised.

DR. WEISS: So we will now go on to other motions, and then on to labeling. Do I have any other motions?

DR. SCHEIN: Yes, I have a motion.

DR. WEISS: Yeah.

DR. SCHEIN: I'd like to propose as a condition that a post- marketing surveillance study involving the collection of new data of content and scope to be determined by the FDA and the Sponsor be required.

DR. WEISS: I think that was what was just --

DR. SCHEIN: No, no. It is a very important distinction. That was follow-up data of the pre-market endothelial cells. I'm referring to post-market surveillance study, as we got a little lecture on from the FDA. And I don't want to spend time, details of the content and scope, that would be worked out between the Sponsor and the FDA.

DR. MATOBA: This is a registry type of --

DR. SCHEIN: I think of half a dozen